STIC Search Report
EIC 3700

STIC Database Tracking Number: 193110

TO: William H Matthews
Location: RND 6b02
Art Unit: 3738

Case Serial Number: 10/763569

From: Jeanne Horrigan
Location: RND 8A34
Phone: 571-272-3529

jeanne.horrigan@uspto.gov

Search Notes

Attached are the search results for the methods for reducing blood reflux or reduce pain in glaucoma implant surgery.

I tagged the references that I thought were most relevant (green tags for claims 1 and/or 2, red tag for claim 11) but I recommend that you review ALL of the results.

Also attached is a search feedback form. Completion of the form is voluntary. Your completing this form would help us improve our search services.

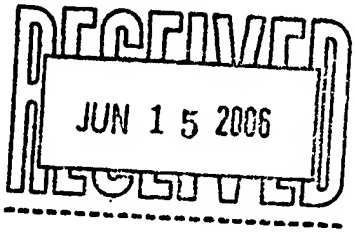
I hope the attached information is useful. Please feel free to contact me if you have any questions or need additional searching on this application.

19311 ϕ

Solomon, Terrance

From: WILLIAM MATTHEWS [william.matthews@uspto.gov]
Sent: Wednesday, June 14, 2006 8:16 PM
To: STIC-EIC3700
Subject: Database Search Request, Serial Number: 10763569

Requester:
WILLIAM MATTHEWS (P/3738)
Art Unit:
GROUP ART UNIT 3738
Employee Number:
78879
Office Location:
RND 06B02
Phone Number:
(571)272-4753
Mailbox Number:



Case serial number:
10763569
Class / Subclass(es):
128/898
Earliest Priority Filing Date:
1/23/03
Format preferred for results:
Paper
Search Topic Information:
see claims 1-14
Special Instructions and Other Comments:

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File 149:TGG Health&Wellness DB(SM) 1976-2006/Jun W2
         (c) 2006 The Gale Group
File 148:Gale Group Trade & Industry DB 1976-2006/Jun 29
         (c)2006 The Gale Group
File  16:Gale Group PROMT(R) 1990-2006/Jun 29
         (c) 2006 The Gale Group
File 160:Gale Group PROMT(R) 1972-1989
         (c) 1999 The Gale Group
File 129:PHIND(Archival) 1980-2006/Jun W4
         (c) 2006 Informa UK Ltd
File 135:NewsRx Weekly Reports 1995-2006/Jun W4
         (c) 2006 NewsRx
File 441:ESPICOM Pharm&Med DEVICE NEWS 2006/Jan W4
         (c) 2006 ESPICOM Bus.Intell.
File 635:Business Dateline(R) 1985-2006/Jun 30
         (c) 2006 ProQuest Info&Learning
File 636:Gale Group Newsletter DB(TM) 1987-2006/Jun 29
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S2     163172   IMPLANT??? OR IMPLANTATION? ? OR STENT??? OR SHUNT???
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             T? ? OR VASOACTIVE()AGONIST? ? OR VASOMODULAT?R? ? OR VASOCON-
             STRICT?R? ? OR VASOPRESS?R? ? OR ALPHA(1W)AGONIST? ? OR BETA(-
             )ADRENERGIC? ?()ANTAGONIST? ?
S4       2104   ANTERIOR()(CHAMBER? ? OR CHAMBRE? ?)
S5        479   TRABECULAR()MESHWORK
S6          5   SCHLEMM? ?()CANAL
S7          2   S1(S)S2(S)S3 [not relevant]
S8          0   S2(S)S3(S)S4:S6

File 155:MEDLINE(R) 1950-2006/Jun 29
         (c) format only 2006 Dialog
File   5:Biosis Previews(R) 1969-2006/Jun W4
         (c) 2006 The Thomson Corporation
File  73:EMBASE 1974-2006/Jun 30
         (c) 2006 Elsevier Science B.V.
File  74:Int.Pharm.Abs 1970-2006/May B2
         (c) 2006 The Thomson Corporation
File  94:JICST-EPlus 1985-2006/Mar W4
         (c)2006 Japan Science and Tech Corp(JST)
File 144:Pascal 1973-2006/Jun W1
         (c) 2006 INIST/CNRS
File 431:MediConf: Medical Con. & Events 1998-2004/Oct B2
         (c) 2004 Dr. R. Steck
File  65:Inside Conferences 1993-2006/Jun 30
         (c) 2006 BLDSC all rts. reserv.
File  35:Dissertation Abs Online 1861-2006/Jun
         (c) 2006 ProQuest Info&Learning
File  34:SciSearch(R) Cited Ref Sci 1990-2006/Jun W4
         (c) 2006 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
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File 6:NTIS 1964-2006/Jun W3
(c) 2006 NTIS, Intl Cpyrght All Rights Res

Set	Items	Description
S1	177439	GLAUCOMA OR (INTRAOCULAR OR INTRA()OCULAR)()PRESSURE OR OCULAR()HYPERTENSION OR HYDROPHTHALMOS
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S3	129364	(VASOCONSTRICTIVE OR VASOPRESSIVE OR VASOMODULATING)()AGENT? ? OR VASOACTIVE()AGONIST? ? OR VASOMODULAT?R? ? OR VASOCONSTRICT?R? ? OR VASOPRESS?R? ? OR ALPHA(1W)AGONIST? ? OR BETA()ADRENERGIC? ?()ANTAGONIST? ?
S4	37119	ANTERIOR()(CHAMBER? ? OR CHAMBRE? ?)
S5	11375	TRABECULAR()MESHWORK
S6	935	SCHLEMM? ?()CANAL
S7	42	S1 AND S2 AND S3
S8	3	S7/2004
S9	13	S7/2005
S10	0	S7/2006
S11	26	S7 NOT S8:S9
S12	18	RD (unique items)
S13	**18**	**Sort S12/ALL/PY,A**
S14	2687	S2 AND S3
S15	0	S14 AND S4 AND S5 AND S6
S16	6	S14 AND S5
S17	25	S14 AND (S4 OR S6)
S18	11	S16:S17 NOT S7
S19	8	RD (unique items)
S20	**8**	**Sort S19/ALL/PY,A**

13/7,K/5 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2006 Elsevier Science B.V. All rts. reserv.
07281562 EMBASE No: 1998150058
Pharmacokinetics of topical beta - adrenergic antagonists **in rabbit aqueous humor evaluated with the microdialysis method**
Ohtori R.; Sato H.; Fukuda S.; Ueda T.; Koide R.; Kanda Y.; Kiuchi Y.; Oguchi K.
R. Ohtori, Department of Ophthalmology, Showa University School of Medicine, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-0064 Japan
Experimental Eye Research (EXP. EYE RES.) (United Kingdom) 1998, 66/4 (487-494)
CODEN: EXERA ISSN: 0014-4835
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39
The microdialysis method was used to evaluate the pharmacokinetics of the **beta - adrenergic antagonists** carteolol and timolol and the new ophthalmic solution WP-934 in rabbit aqueous humor, following instillation. A probe with a microdialysis membrane (length, 5 mm; diameter, 0.2 mm) was **implanted** in the **anterior** chamber of the pigmented rabbit and perfused with Ringer's solution. Twenty microliters of 0.5% timolol maleate (0.5% Timoptol(R)), 2% carteolol hydrochloride (2% Mikelan(R)), or a novel preparation of 0.5% timolol maleate (WP-934) that gels after instillation were then instilled. The concentrations of these drugs in dialysates were measured using high- performance liquid chromatography and an electrochemical detection system. In vitro relative recovery of the membrane with timolol and carteolol was approximately 17.5% and 21.6%,

respectively. Timolol and carteolol levels in aqueous humor increased rapidly after instillation of Timoptol and Mikelan and reached maximal levels (C(max)) within 60 minutes. The C(max) of carteolol (4.25 mug mlsup -sup 1) was lower than that of timolol (5.52 mug mlsup - sup 1), suggesting that the corneal permeability of timolol is higher than that of carteolol. After instillation of WP-934, the C(max) of timolol (12.32 mug mlsup -sup 1) was 2-2-fold higher than that after instillation of Timoptol. However, t(1/2) values of **beta - adrenergic antagonists** after instillation of the three preparations were not significantly different. These data suggest that the microdialysis technique is useful for continuous monitoring of aqueous levels of **beta**-blockers and for analysis of their pharmacokinetic parameters while requiring much fewer animals than conventional sampling with paracentesis.
MEDICAL DESCRIPTORS:
*aqueous humor; *drug monitoring; *microdialysis; * **glaucoma**

13/7,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11734834 PMID: 9547698
Evaluation of microdialysis sampling of aqueous humor for in vivo models of ocular absorption and disposition.
Rittenhouse K D; Peiffer R L; Pollack G M
Division of Pharmaceutics, School of Pharmacy, University of North Carolina, Chapel Hill 27599-7360, USA.
Journal of pharmaceutical and biomedical analysis (ENGLAND) Feb 1998, 16 (6) p951-9, ISSN 0731-7085--Print Journal Code: 8309336
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
The dynamics of **beta**-adrenergic-associated reductions in aqueous humor production for treatment of elevated **intraocular pressure** are not well understood. In particular, the relationship between **ocular** pharmacokinetics and pharmacodynamics has yet to be established. This study was undertaken to develop a procedure for examining the **ocular** absorption and disposition of topically administered ophthalmic **beta - adrenergic antagonists** in individual animals. Dogs were anesthetized with isoflurane and a microdialysis probe was **implanted** in the **anterior** chamber of one eye and perfused with 0.9% saline at a rate of 2 microliters min-1. 3H-propranolol was administered by intracameral injection or topically. Each dog received intracameral and topical propranolol, in alternate eyes on separate days, in a randomized cross-over fashion. Microdialysis probe effluent was collected every 5 min for > or = 2.5 h; concentrations of propranolol were determined by liquid scintillation spectroscopy and were corrected for probe recovery of the substrate as determined by in vivo retrodialysis (approximately 46%) to estimate aqueous humor concentrations. In separate experiments in rabbits, microdialysis probes were **implanted** in each eye. 3H-propranolol was administered topically to one eye; the contralateral eye received intracameral 3H-propranolol. Model-independent pharmacokinetic parameters for each treatment phase were calculated. The mean +/- S.D. times to peak concentration of propranolol in aqueous humor were 86.6 +/- 47.6 min in the dog and 54.1 +/- 20.4 min in the rabbit. The terminal rate constant was 0.0189 +/- 0.00429 min-1 in the dog vs. 0.00983 +/- 0.00546

min-1 in the rabbit. **Intraocular** tissue availability of propranolol differed markedly between the dog (n = 3) and rabbit (n = 3) (approximately 0.056 in the dog vs. approximately 0.55 in the rabbit). These results demonstrate the utility of microdialysis sampling for examination of **ocular** pharmacokinetics.
Record Date Created: 19980615
Record Date Completed: 19980615

13/7,K/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.
12108382 PMID: 10551304
Inverted U' strategy for short pulsed laser posterior capsulotomy.
Zeki S M
Birmingham and Midland Eye Center, UK.
Acta ophthalmologica Scandinavica (DENMARK) Oct 1999, 77 (5) p575-7, ISSN 1395-3907--Print Journal Code: 9507578
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Pit marks and cracks in the axial region of the optic of **intraocular implants** (IOL) in the pseudophakic eye are a frequent clinical observation and follow Nd:YAG laser posterior capsulotomy procedures. A new technique is presented for carrying out YAG capsulotomy without risking damage to the axial part of the optic. This technique has been used successfully on 200 eyes. It makes use of the fact that an opacified posterior capsule reacts to disruption by retracting. This treatment strategy simply directs this process of retraction to create a 3 mm gap in the axial region without having to treat this area.
Record Date Created: 19991215
Record Date Completed: 19991215
; Acetazolamide--therapeutic use--TU; Adrenergic **alpha** - **Agonists** --therapeutic use--TU; Clonidine--analogs and derivatives--AA; Clonidine --therapeutic use--TU; Humans; **Intraocular Pressure** --drug effects--DE; Lenses, **Intraocular**; Medical Illustration; Pilot Projects; Postoperative Period; Reoperation
Chemical Name: Adrenergic **alpha** - **Agonists** ; Clonidine; Acetazolamide; apraclonidine

13/7,K/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.
12757391 PMID: 10865991
Pharmacodynamics of beta-blocker modulation of aqueous humor production.
Rittenhouse K D; Pollack G M
Preclinical Sciences, Bausch & Lomb Pharmaceuticals, Tampa, FL 33637, USA.
Experimental eye research (ENGLAND) Apr 2000, 70 (4) p429-39, ISSN 0014-4835--Print Journal Code: 0370707
Contract/Grant No.: 1RO3 AG15283-01; AG; NIA
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH

Main Citation Owner: NLM
Record type: MEDLINE; Completed
A conscious rabbit model with microdialysis sampling of endogenous aqueous humor ascorbate was developed in order to assess the pharmacodynamics of **beta**-blocker modulation of aqueous humor production. CMA/20 microdialysis probes were **implanted** in the **anterior** chamber of each eye of rabbits (n = 6). After a 2 week recovery period, an i.v. bolus of 14C-ascorbate (20 microCi) was administered. Blood samples and aqueous humor microdialysis probe effluent were collected and analysed for endogenous and 14C-ascorbate to estimate the basal rate of ascorbate blood to aqueous humor secretion (Ro). After a 1 hr washout, each rabbit received a series of three doses of 3H-propranolol (750-3000 microg, 16.5 microCi mg(-1)) every 60 min into the lower cul-de-sac of each eye. Probe effluent was analysed for endogenous ascorbate and 3H-propranolol; ascorbate and propranolol in the iris/ciliary body, vitreous and aqueous was determined at the end of the experiment. Nonlinear least-squares regression analysis of the concentration-time profiles for aqueous humor ascorbate was performed to estimate the change in aqueous humor flow. The average basal aqueous humor ascorbate secretion rate was approximately 48/microg hr(-1). Propranolol (1500 microg) produced significant increases in aqueous humor ascorbate, this observation is consi**stent** with a reduction in aqueous humor production (approximately 47%). Analysis of **intraocular** tissue ascorbate indicated that propranolol inhibited ascorbate secretion at the 3000 microg dose, the highest dose examined in this study; this inhibition was not observed at the 750 microg or 1500 microg doses. Changes in aqueous humor production precipitated by the administration of **beta-adrenergic antagonists** can be estimated by measuring changes in aqueous humor ascorbate concentrations in the conscious rabbit. Microdialysis sampling of aqueous humor for endogenous ascorbate provides a relevant analytic tool to estimate modulatory effects of anti-**glaucoma** drugs on aqueous humor production.
Record Date Created: 20000707
Record Date Completed: 20000707

13/7,K/14 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

11868962 EMBASE No: 2002441181
Primary open-angle glaucoma
Goldberg I.; Graham S.L.; Healey P.R.
Dr. I. Goldberg, Sydney Eye Hospital, Sydney, NSW Australia
Medical Journal of Australia (MED. J. AUST.) (Australia) 18 NOV 2002
, 177/10 (535-536)
CODEN: MJAUA ISSN: 0025-729X
DOCUMENT TYPE: Journal ; Editorial
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 9
MEDICAL DESCRIPTORS:
*open angle **glaucoma** --epidemiology--ep; *open angle **glaucoma** --drug therapy--dt; *open angle **glaucoma** --surgery--su
...factor; prevalence; visual field defect; visual acuity; long term care; patient compliance; trabeculoplasty; laser surgery; **intraocular pressure** ; treatment failure; **glaucoma** drainage **implant** ; blindness; monitoring; perimetry; editorial
DRUG TERMS (UNCONTROLLED): prostaglandin F2 **alpha agonist**--drug therapy--dt

13/7,K/16 (Item 16 from file: 94)
DIALOG(R)File 94:JICST-EPlus

05494199 JICST ACCESSION NUMBER: 03A0501205 FILE SEGMENT: JICST-E
Outcome of surgery for elevated intraocular pressure following cataract surgery with ruptured posterior capsule.
SAITO YASUKO (1); TAKEUCHI ATSUSHI (1); NAKAMURA SACHIO (1); MIZUTANI MASAHIRO (1); MIYAKE GOICHIRO (1); IKAGAWA HIROSHI (1); KOIKE NOBUKO (1); HISADA YOSHIAKI (1); IWAKI MASAYOSHI (1)
(1) Aichiidai Ganka
Rinsho Ganka(Japanese Journal of Clinical Ophthalmology), 2003, VOL.57,NO.6 , PAGE.1021-1024, REF.8
JOURNAL NUMBER: Z0515BAJ ISSN NO: 0370-5579
UNIVERSAL DECIMAL CLASSIFICATION: 617.7-089
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: Surgical intervention became necessary for persistently elevated **intraocular pressure** (IOP) following cataract surgery with ruptured posterior capsule in 6 eyes of 6 patients. The cause of elevated IOP could be identified in 3 eyes. Viscoelastic material in the **anterior** chamber, fall of lens nucleus into the vitreous, and hyphema with inflammation in one eye each. In these 3 eyes, the IOP became normalized after the cause was surgically eliminated. In the other 3 eyes, pseudoexfoliation was present in one eye and no apparent cause could be identified in 2 eyes. These 3 eyes necessitated **glaucoma** surgery. Cataract surgery on high-risk eyes need particular care to avoid postoperative **ocular hypertension** . (author abst.)
DESCRIPTORS: **ocular hypertension** ; ...
... **intraocular pressure** ; ...
... **beta adrenergic antagonist** ;
...BROADER DESCRIPTORS: artificial **implant** ;

20/7,K/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03454532 Genuine Article#: PF955 Number of References: 33
Title: TRANSPLANTATION OF ENCAPSULATED BOVINE CHROMAFFIN CELLS IN THE SHEEP SUBARACHNOID SPACE - A PRECLINICAL STUDY FOR THE TREATMENT OF CANCER PAIN
Author(s): JOSEPH JM; GODDARD MB; MILLS J; PADRUN V; ZURN A; ZIELINSKI B; FAVRE J; GARDAZ JP; MOSIMANN F; SAGEN J; CHRISTENSON L; AEBISCHER P
Corporate Source: CHU VAUDOIS,DIV RECH CHIRURG,PAVILLON 3/CH-1011LAUSANNE//SWITZERLAND/; UNIV LAUSANNE,CHU VAUDOIS,SCH MED,DIV AUTONOME RECH CHIRURG/LAUSANNE//SWITZERLAND/; BROWN UNIV,ARTIFICIAL ORGANS BIOMAT & CELLULAR TECHNOL SECT/PROVIDENCE//RI/02912; CHU VAUDOIS,SERV NEUROCHIRURG/CH-1011 LAUSANNE//SWITZERLAND/; CHU VAUDOIS,ANESTHESIOL SERV/CH-1011 LAUSANNE//SWITZERLAND/; CHU VAUDOIS,SERV CHIRURG/CH-1011 LAUSANNE//SWITZERLAND/; UNIV ILLINOIS,DEPT ANAT & CELL BIOL/CHICAGO//IL/00000; CYTO THERAPEUT INC/PROVIDENCE//RI/00000
Journal: CELL TRANSPLANTATION, 1994, V3, N5 (SEP-OCT), P355-364
ISSN: 0963-6897

Language: ENGLISH Document Type: ARTICLE
Abstract: Chromaffin cells have been shown to release a combination of pain-reducing neuroactive compounds including catecholamines and opioid peptides. The allogeneic transplantation of chromaffin cells in the subarachnoid space has been shown to alleviate pain in various rodent models and possibly in terminal cancer patients. Because of the shortage of human cadaver donor tissue, we are investigating the possibility of transplanting xenogeneic cells in polymer capsules. In this technique, cells are surrounded by a permselective synthetic membrane whose pores are suitably sized to allow diffusion of nutrients, neurotransmitters and growth factors, but restrict the diffusion of the large molecules of the immune system and prevent contact with immunocompetent cells. The encapsulation technique therefore allows transplantation of xenogeneic tissue between species as well as retrieval of transplanted cells. Previously we have reported that encapsulated bovine chromaffin cells survive and alleviate pain in various rodent models. The purpose of the present study was to assess the feasibility of **implanting** a human sized device in a large animal model. Adrenals from 5 calves were surgically removed; chromaffin cells were isolated from these glands using a collagenase-based digestion-filtration technique. Cells were loaded into acrylic-based tubular (5 cm long, 920 mu m wide) permselective capsules attached to silicone tethers. The capsules were maintained in vitro for at least 7 days following the encapsulation procedure. Nicotine evoked release was analyzed in a defined subgroup from each batch. One capsule was then **implanted** using a guiding cannula system in the lumbar subarachnoid space of each sheep for 4 (n = 5) and 8 (n = 1) wk. All capsules were retrieved intact by gentle pulling on the silicone tether. Except for one capsule, the evoked catecholamine release of the retrieved capsules was in the same range as that of other capsules from the same cohort that had been maintained in vitro. All retrieved capsules were devoid of host fell reaction. Clusters of viable cells dispersed in an alginate immobilizing matrix were observed throughout all the **implanted** capsules. This study demonstrates the feasibility of transplanting functional encapsulated xenogeneic chromaffin cells into the cerebrospinal fluid of a large animal model using a capsule of appropriate dimensions for human **implants** . We believe that these results suggest the appropriateness of human clinical trials in patients suffering from refractory terminal cancer pain.
Research Fronts: 92-1820 001 (INDUCTION OF **ANTERIOR CHAMBER** -ASSOCIATED IMMUNE DEVIATION; **INTRAOCULAR** TRANSFORMING GROWTH-FACTOR-**BETA**; CILIARY BODY CELLS; IMMUNOREGULATORY MECHANISMS)
92-4928 001 (INTRATHECAL CLONIDINE; SPINAL **ALPHA** -2 **AGONISTS** ; CHRONIC PAIN IN RATS; BUPIVACAINE FOR POSTOPERATIVE ANALGESIA)

20/7,K/3 (Item 3 from file: 35)
DIALOG(R)File 35:Dissertation Abs Online

01807750 ORDER NO: AADAA-I9938210
Beta-blocker modulation of aqueous humor production
Author: Rittenhouse, Kay Doris
Degree: Ph.D.
Year: 1999
Corporate Source/Institution: The University of North Carolina at Chapel Hill (0153)
Adviser: Gary M. Pollack

Source: VOLUME 60/07-B OF DISSERTATION ABSTRACTS INTERNATIONAL.
PAGE 3233. 208 PAGES
ISBN: 0-599-39506-0

Purpose. A conscious rabbit model with microdialysis sampling of aqueous humor (AH) for the assessment of the pharmacokinetics and pharmacodynamics of anti**glaucoma** drugs was developed. Detailed examination of the modulatory effects of **beta-adrenergic antagonists** on AH formation was conducted using <super>3</super>H-propranolol as a pharmacodynamic probe and ascorbate as an endogenous AH turnover marker. *Methods*. (1) Examination of the effects of anesthesia and nonstationary protein binding on the **ocular** pharmacokinetics of propranolol was conducted in anesthetized and conscious rabbits following microdialysis probe **implantation** in the **anterior chamber**. **Ocular** pharmacokinetic parameters for each group were compared and contrasted. (2) The uptake-kinetics of AH ascorbate was assessed by microdialysis sampling of posterior versus **anterior chamber** AH following systemic administration of <super>14</super>C-labelled and unlabelled ascorbate in conscious rabbits. Nonlinear least-squares regression analyses developed from complex pharmacoldnetic modeling schemes for serum and AH ascorbate concentration-time data were performed to estimate the kinetics of ascorbate, blood to aqueous transport. (3) Microdialysis probes were **implanted** in the **anterior chamber** of each eye of six rabbits. A series of propranolol doses was administered to each eye according to an hourly regimen (3 doses: 750-μg to 3000-μg). Microdialysate was collected for up to 7hr post-dose and assayed for ascorbate (UV-spectrophotometry) and <super>3</super>H-propranolol (liquid-scintillation spectroscopy) concentrations in AH and **intraocular** tissues. Nonlinear least-squares regression analysis of ascorbate concentration-time data was used to estimate the %reduction in AH production as a function of the propranolol dose. *Results*. Anesthesia (□8-fold higher exposure) and nonstationary protein binding (□1.9-fold lower exposure) altered the **intraocular** pharmacokinetics of propranolol. Ascorbate blood-to-aqueous transport was characterized by linear-uptake and efflux clearances into and out of posterior aqueous (in contrast to previously reported results) at physiologically relevant blood concentrations and linear translocation and efflux constants between **intraocular** compartments. A U-shaped dose-response relationship was observed for propranolol inhibition of AH production; no changes to ascorbate AH time-course were observed for the 750-μg and 3000-μg doses; in contrast, a □50% reduction in AH flow was observed for the 1500-μg dose. *Conclusions*. Microdialysis sampling of AH ascorbate and propranolol, was successful in evaluating the **ocular** pharmacokinetics and pharmacodynamics of **beta-adrenergic antagonists** in reducing AH formation.

20/7,K/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012024266 BIOSIS NO.: 199900283926
Microdialysis evaluation of the ocular pharmacokinetics of propranolol in the conscious rabbit
AUTHOR: Rittenhouse Kay D; Peiffer Robert L Jr; Pollack Gary M (Reprint)
AUTHOR ADDRESS: Division of Drug Delivery and Disposition, School of Pharmacy, University of North Carolina, Chapel Hill, NC, 27599-7360, USA **USA
JOURNAL: Pharmaceutical Research (New York) 16 (5): p736-742 May, 1999 1999
MEDIUM: print

ISSN: 0724-8741
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: Purpose. This study was conducted to assess the effects of anesthesia and aqueous humor protein concentrations on **ocular** disposition of propranolol. Methods. Rabbits were anesthetized and a microdialysis probe was inserted into the **anterior chamber** of one eye; the contralateral eye served as a control. At timed intervals after probe placement, a 100-mul sample of aqueous humor was aspirated from each eye to determine protein concentration. In vitro protein binding parameters were used to simulate the impact of protein concentration on propranolol disposition. To assess the influence of anesthesia, probes were **implanted** in the **anterior chamber** of each eye. After >5-day stabilization, conscious and anesthetized rabbits (n = 3/group) received a 200-mug topical dose of (3H)DL-propranolol in each eye; propranolol was assayed in probe effluent. Results. Changes in aqueous humor protein concentrations were observed following probe insertion. Simulations demonstrated that the unbound propranolol AUC (apprx2.4-fold) in aqueous humor should be reduced due to protein influx. **Intraocular** propranolol exposure in anesthetized rabbits was apprx8-fold higher than in conscious rabbits, and apprx1.9-fold higher than in rabbits without a post-surgical recovery period. Conclusions. Anesthesia and time-dependent aqueous humor protein concentrations may alter **ocular** pharmacokinetics, and must be taken into account in the design of microdialysis experiments.
DESCRIPTORS:
CHEMICALS & BIOCHEMICALS: ...cardiovascular-drug, **beta - adrenergic antagonist** , disposition, **ocular** pharmacokinetics

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File 350:Derwent WPIX 1963-2006/UD,UM &UP=200641
         (c) 2006 The Thomson Corp.
File 347:JAPIO Dec 1976-2005/Dec(Updated 060404)
         (c) 2006 JPO & JAPIO
Set     Items   Description
S1       7770   GLAUCOMA OR (INTRAOCULAR OR INTRA()OCULAR)()PRESSURE OR OC-
             ULAR()HYPERTENSION OR HYDROPHTHALMOS
S2     185446   IMPLANT??? OR IMPLANTATION? ? OR STENT??? OR SHUNT???
S3       1687   (VASOCONSTRICTIVE OR VASOPRESSIVE OR VASOMODULATING)()AGEN-
             T? ? OR VASOACTIVE()AGONIST? ? OR VASOMODULAT?R? ? OR VASOCON-
             STRICT?R? ? OR VASOPRESS?R? ? OR ALPHA(1W)AGONIST? ? OR BETA(-
             )ADRENERGIC? ?()ANTAGONIST? ?
S4        817   ANTERIOR()(CHAMBER? ? OR CHAMBRE? ?)
S5        130   TRABECULAR()MESHWORK
S6         27   SCHLEMM? ?()CANAL
S7      13018   IC=A61F-009?
S8         21   S1 AND S2 AND S3
S9          2   S2 AND S3 AND S4:S6
S10        21   S8:S9

10/26,TI/16     (Item 16 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2006 The Thomson Corp. All rts. reserv.
015583694
WPI Acc No: 2003-645851/200361
  Composition useful for treating e.g. glaucoma comprises substituted
  5-hydroxy indole compounds and an excipient

 10/34/13     (Item 13 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2006 The Thomson Corp. All rts. reserv.
016446248
WPI Acc No: 2004-604164/200458
  Sustained release drug delivery device, useful for the treatment and/or
  prevention of raised intraocular pressure , comprises an inner drug
  core comprising at least one adrenergic agent and a coating layer
Patent Assignee: CONTROL DELIVERY SYSTEMS INC (CONT-N)
Inventor: ASHTON P; GUO H
Number of Countries: 109  Number of Patents: 004
Patent Family:
Patent No     Kind   Date     Applicat No    Kind   Date     Week
WO 200466979   A2  20040812  WO 2004US1718   A   20040123  200458  B
AU 2004207506  A1  20040812  AU 2004207506   A   20040123  200557
EP 1592408     A2  20051109  EP 2004704837   A   20040123  200573
                               WO 2004US1718   A   20040123
MX 2005007719  A1  20051001  WO 2004US1718   A   20040123  200620
                               MX 20057719     A   20050720
Priority Applications (No Type Date): US 2003501974 P 20030911; US
  2003442499 P 20030124; US 2003482677 P 20030626; US 2003483316 P 20030626
Patent Details:
Patent No  Kind Lan Pg   Main IPC     Filing Notes
WO 200466979  A2 E  49 A61K-009/22
   Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ
   CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID
   IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
   NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ
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UA UG US UZ VC VN YU ZA ZM ZW
Designated States (Regional): AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
AU 2004207506 A1 A61K-009/22 Based on patent WO 200466979
EP 1592408 A2 E A61K-009/22 Based on patent WO 200466979
Designated States (Regional): AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
MX 2005007719 A1 A61K-009/22 Based on patent WO 200466979
Abstract (Basic): WO 200466979 A2

NOVELTY - A sustained release drug delivery device (adapted for insertion or **implantation** in or adjacent to the eye) comprises:

(a) an inner drug core (I) comprising at least one adrenergic agent (II); and

(b) a coating layer (III) on the surface of (I) that is substantially impermeable or partially or substantially permeable to the passage of (II) and has openings that permit the diffusion of (II

DETAILED DESCRIPTION - A sustained release drug delivery device (adapted for insertion or **implantation** in or adjacent to the eye) comprises:

(a) an inner drug core (I) comprising at least one adrenergic agent (II); and

(b) a coating layer (III) on the surface of (I) that is substantially impermeable or partially or substantially permeable to the passage of (II) and has openings that permit the diffusion of (II).

The coating layer is substantially insoluble and inert in body fluids and compatible with body tissues. It produces, when inserted or **implanted** , a substantially constant rate of release of agent (II) from the device.

An INDEPENDENT CLAIM is also included for the administration of at least one adrenergic agent (II) to the ciliary body of an eye, which comprises **implanting** a device as above in or adjacent to the eye. The device delivers (II) so that the concentration of (II) in the ciliary body is maintained at a therapeutically effective concentration for a period of at least 360 days (preferably 30 days).

ACTIVITY - Ophthalmological; Hypotensive.

No details of tests for ophthalmological activity are given.

MECHANISM OF ACTION - **beta** - **Adrenergic antagonist** ; **alpha1**-adrenoceptor agonist; **alpha2**-adrenoceptor agonist.

USE - The device is useful for the treatment and/or prevention of raised **intraocular pressure**, such as that associated with **glaucoma**.

ADVANTAGE - The device is useful to treat **glaucoma** without adverse side effects.

pp; 49 DwgNo 0/5

Technology Focus:

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Device: If the coating layer is substantially impermeable to the passage of (II), the device may also include additional coatings (IV) that are permeable to the passage of (II), and which are substantially insoluble and inert in body fluids and compatible with body tissues. Coatings (III) and (IV) produce, when **implanted** , a substantially constant rate of release of (II) from the device. Coating (III) has sufficient dimensional stability to be filled with the drug core without changing its shape.

The core (I) is preferably admixed with a polymer matrix (preferably a bioerodible matrix) and the device is formed by co-extruding (I) and (III).

Preferred Components: The adrenergic agent (II) is brimonidine, aapraclonidine (sic), bunazosin, timolol, **beta**xolol, levo**beta**xolol, levobunolol, carteolol, isoprenaline, fenoterol, metipranolol, clenbuterol, epinephrine or dipivefrin
Extension Abstract:
ADMINISTRATION - Administration of (II) is **intraocular**. No dosage given.
Derwent Class: B05; B07
International Patent Class (Main): A61K-009/22

10/34/20 (Item 20 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2006 The Thomson Corp. All rts. reserv.
014920122 **Image available**
WPI Acc No: 2002-740829/200280
Delivery of therapeutic agent locally to eye for treating e.g. uveitis and glaucoma, involves attaching a controlled release ocular implant to eye tissues
Patent Assignee: US DEPT HEALTH & HUMAN SERVICES (USSH); CSAKY K G (CSAK-I); NUSSENBLATT R B (NUSS-I); ROBINSON M R (ROBI-I); SMITH J A (SMIT-I); SUNG C (SUNG-I); YUAN P (YUAN-I); FRONHEISER M P (FRON-I); KIM H (KIMH-I)
Inventor: CSAKY K G; FRONHEISER M P; KIM H C; NUSSENBLATT R B; ROBINSON M R ; SMITH J A; SUNG C; YUAN P; KIM H
Number of Countries: 101 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200274196	A1	20020926	WO 2002US7836	A	20020314	200280	B
US 20030175324	A1	20030918	US 2001808149	A	20010315	200362	
EP 1377232	A1	20040107	EP 2002723446	A	20020314	200404	
			WO 2002US7836	A	20020314		
US 6713081	B2	20040330	US 2001808149	A	20010315	200423	
AU 2002254225	A1	20021003	AU 2002254225	A	20020314	200432	
US 20040180075	A1	20040916	WO 2002US7836	A	20020314	200461	
			US 2004471468	A	20040503		

Priority Applications (No Type Date): US 2001808149 A 20010315
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200274196	A1	E	89	A61F-002/00	

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

US 20030175324	A1	A61F-002/00	
EP 1377232	A1 E	A61F-002/00	Based on patent WO 200274196

Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

US 6713081	B2	A61F-002/00	
AU 2002254225	A1	A61F-002/00	Based on patent WO 200274196
US 20040180075	A1	A61F-002/00	

Abstract (Basic): WO 200274196 A1
NOVELTY - A therapeutic agent (12) (TA) is delivered to an eye, by

attaching an **implant** (10) containing TA to eye tissues in which the **implant** releases TA continuously by initial delivery of a loading dose followed by a period of time in which the TA is delivered at a relatively constant rate.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) A controlled release **ocular implant** , comprising composite material matrix layer (CMML) including TA-I, and polymeric matrix material (PMM) (14) dispersed with TA-I. PMM includes a biodegradable polymer permeable to TA, and a water-soluble polymer having greater water solubility than the permeable polymer;

(2) **Implant** formation involving forming pre-mixture by mixing and dispersing TA with a cellulose ether polymer in an aqueous medium, combining pre-mixture with super hydrolyzed polyvinyl alcohol, and coating on flat surface, optionally embedding TA pellet within coating layer, drying, and cutting to provide an **ocular implant** ;

(3) An **intraocular** reservoir **implant** comprising TA-I reservoir sub-assembly including an inner core of TA covered by and radially centered within a polymeric layer including silicon material permeable to TA and an **ocular** attachment unit; and

(4) Production of **intraocular implant** (IOI) involving introducing flowable silicone fluid (SF) into an impression in upper surface (including polytetrafluoroethylene) of mold, centering drug pellet submerged in SF, hardening SF to integral silicone/pellet subassembly, and separating from mold upper surface.

ACTIVITY - Ophthalmological; antiinflammatory. No test details are given for the above mentioned activity.

MECHANISM OF ACTION - None given in source document.

USE - For delivering TA to eye locally by attaching the **implant** to eye tissues such as subconjunctival tissues and intravitreal tissues, for treating uveitis, age-related macular degeneration, choroidal neovascular membranes (CNVM), and **glaucoma** , in human and veterinary applications. The **implant** is attached to a subconjunctival region for corneal allograft therapy, or intravitreal region for treatment of CNVM. The **implant** delivers leflunomide for treating uveitis.

ADVANTAGE - Super hydrolyzed PVA prevents **implant** from being extruded, and also permits more predictable pharmacokinetic behavior of the device. The **implants** are highly versatile and can be tailored to enhance the delivery regimen both in terms of administration mode(s) and type(s) of drugs delivered. The **implant** permits continuous release of therapeutic agents into the eye over a specified period of time (weeks, months or year). The **implant** system requires intervention only for initiation and termination of the therapy. Patient compliance issues during a regimen are eliminated. The time-dependent delivery of drugs to the eye makes it possible to maximize the pharmacological and physiological effects of the eye treatment.

DESCRIPTION OF DRAWING(S) - The figure shows an enlarged view of a sustained release, subconjunctival matrix single mode **implant** device.

Implant (10)
Therapeutic agent (12)
Polymeric matrix material (14)
pp; 89 DwgNo 1/21

Technology Focus:

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred

Properties: The constant release rate, which occurs for 3-6 months or more, is a maintenance dosage. The therapeutic agent is antibiotic, antibacterial, antiviral, anti- **glaucoma** , antiallergic, antiinflammatory, anti-angiogenesis, antiproliferative, immunomodulatory, anticancer, antisense, antimycotic, mycotic, anticholinesterase, mydriatic, differentiation modulators, sympathomimetics, anesthetics, **vasoconstrictors** , vasodilators, decongestants, polypeptides, proteins, steroids, carbonic anhydride inhibitors, polycations, polyanions, and/or lubricating agents. The therapeutic agent is especially cyclosporin or 2-methoxyestradiol.

Preferred **Implant** : A discrete solid core containing TA delivers as an initial loading dose delivery followed by sustained release of a lower, relatively constant rate of infusion. The solid core is embedded within CMML. The attachment unit in IOI, is a suture stub including a cross-linked polyvinyl alcohol member and is attached to the polymeric layer by an adhesive (permeable to TA dispersion). IOI includes a discrete inlay member including TA, attached to adhesive. IOI further includes TA reservoir assembly **implant** (TA-RAI)-II containing TA different from TA-RAI-I. A silk mesh fabric is embedded in the silicone at one end of the **implant** .

POLYMERS - Preferred Composition: CMML contains (wt.%) permeable polymer (5-50) including super hydrolyzed polyvinyl alcohol, water-soluble polymer (0.05-90) including cellulose ether polymer and TA (1-50). The pre-mixture is combined with (wt.%) super hydrolyzed polyvinyl alcohol (6-50), cellulose ether polymer (0.05-90), TA (1-50) and water (balance amount).

Preferred Components: The cellulose ether polymer includes hydroxy alkyl cellulose e.g. hydroxy propyl methyl cellulose. A part of the exterior surface area of the composite material matrix is covered by polymethyl methacrylate for adjusting the rate of delivery of TA from **implant** . PMM includes poly(ethylene vinyl)acetate and a cellulose ether polymer.

Extension Abstract:

EXAMPLE - 4.5 g of super hydrolyzed polyvinyl alcohol (PVA) was added to 30 ml of water, placed in beaker of boiling water, centrifuged and 15 weight% (wt.%) solution of super hydrolyzed polyvinyl alcohol was obtained. Separate pre-mixtures were prepared using cyclosporine A (CsA). The therapeutic agents were separately premixed in a solution of Methocel E4M (hydroxy propyl methyl cellulose (HPMC)) (0.05 wt.%). 500 mg of drug was mixed with 2.25 g of HPMC. The super hydrolyzed PVA solution was combined with HPMC/drug mixture, blended and centrifuged. The mixtures was injected between two glass plates with 1-5 mm space, cooled, dried to make dual mode subconjunctival matrix **implants** , compressed into pellets, and embedded within coating layer. The slab was dried, and trephine was used to make the **implants** . The matrix **implants** were subjected to in vitro release rates of single and dual mode CsA **implants** . The single mode matrix **implant** produced an initial loading dose of CsA (125.54+/-1.47 microg/day) with a logarithmic decline to less than 0.5 microg/day by day 31. Daily release rates reached a steady state release of 6 microg/day after day 40 and the release rates were predicted to be stable for 18 months. The single mode matrix **implant** delivered potentially therapeutic levels of CsA to eye for a month. A dual mode matrix **implant** delivered an initial loading dose of CsA which lasted for a month followed by a steady state sustained-release delivery of CsA as a maintenance dose for at least 1 year. The **implants** were found to be safe by

histopathological examination and by electroretinography.
Derwent Class: A96; B05; B07; D22; P32
International Patent Class (Main): A61F-002/00

10/34/21 (Item 21 from file: 350)
DIALOG(R)File 350:Derwent WPIX

014397518 **Image available**
WPI Acc No: 2002-218221/200228
Implant especially for the treatment of glaucoma comprises removable peduncular body for insertion in the eye
Patent Assignee: SCHRAGE N (SCHR-I)
Inventor: KAMPMEIER J; LANG G K; SCHRAGE N; SCHUETTE E
Number of Countries: 001 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
DE 19947711	A1	20010503	DE 1047711	A	19991004	200228	B
DE 19947711	B4	20040212	DE 1047711	A	19991004	200412	

Priority Applications (No Type Date): DE 1047711 A 19991004
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
DE 19947711	A1		6	A61F-002/14	
DE 19947711	B4			A61F-002/14	

Abstract (Basic): DE 19947711 A1

NOVELTY - An **implant**, especially for use in **glaucoma** therapy, comprises a peduncular body which can be inserted in and removed from an orifice in the eye.

ACTIVITY - Ophthalmological.

No biological data given.

MECHANISM OF ACTION - None given.

USE - The **implant** is useful for the treatment of **glaucoma** .

ADVANTAGE - Use of the **implant** provides improved **intraocular** drainage and healing compared with prior art procedures, e.g. erbium-YAG-laser treatment.

DESCRIPTION OF DRAWING(S) - The drawing shows an eye with an inserted **implant** . (Drawing includes non-English language text).

pp; 6 DwgNo 1/2

Technology Focus:

TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred **Implant** : The peduncular body has one flat side and is otherwise preferably conical with a length of 0.1-30 mm, especially 2-10 mm, and a diameter of 0.01-1.5 mm, especially 0.1-0.6 mm. The body has lateral extensions, which act as **intraocular** supports, at least in a region turned to the front of the eye. It also has a specially curved or bent shape in the region of one end. Further, the body has a flat, leaf or heart-shaped region, preferably 2-150 mm2, especially 20-40 mm2, symmetrically arranged with respect to the axis of the body.

The **implant** has at least one lug and/or reinforcing rib. Small peduncular protuberances for microsurgical attachment to a vessel or containing fibres for strengthening or a wick are also suitably present.

Also, the **implant** has at least one internal channel leading from the **implantation** opening to the into the binding tissue. At least one of these channels contains a wick for the directed transport of substances from or into the eye. The **implant** is made from a

resorbable material, e.g. poly-D,L-lactide, polyglycol lactide, gelatine or a sugar polymer, or from a non-resorbable material, e.g. titanium, a silicone, polyvinyl alcohol or a polymethacrylate, polyhydroxymethyl methacrylate or polyvinyl difluoride.

The **implant** surface is coated with a bioactive substance, especially for the prevention or modelling of scar formation or the avoidance of cyst formation.

These substances include laminin, fibronectin, 5-fluorouracil, a hirudin, heparan sulfate, endothelin, tissue plasminogen activator or a steroid. The **implant** contains an arrangement, especially in the form of pores, for the release of drugs by an immediate or delayed release method.

Typical methods include depot-wick and micropump systems. This arrangement is preferably situated in at least partly degradable regions of the **implant** .

The drug is especially an lanatoprost, an azetazolamide or pilocarpine derivative, dorzolamide, a **beta**-blocker, **alpha** - **agonist** or -antagonist, 5-fluorouracil, an antimetabolite, antiinfective, e.g. a virustatic, antibiotic or antimycotic, an antihistamine, steroid or antiinflammatory.

The **implant** contains a micropump system for the removal of water from the eye chamber. Also, it contains a micro-**pressure** and/or tension sensor for the telemetric transmission of eye **pressure** data to a receiver. An antenna or energy transducer associated with an external sensor and/or energy source is typically also present for use in the application of stimuli to the eye.

POLYMERS - Preferred Components: The **implant** is made from poly-D,L-lactide, polyglycol lactide, gelatine, a sugar polymer, a silicone, polyvinyl alcohol or a polymethacrylate, polyhydroxymethyl methacrylate or polyvinyl difluoride.

INORGANIC CHEMISTRY - Preferred Components: The **implant** is made from titanium.

PHARMACEUTICALS - Preferred Components: The **implant** surface is coated with laminin, fibronectin, 5-fluorouracil, a hirudin, heparan sulfate, endothelin, tissue plasminogen activator or a steroid.

The **implant** contains an arrangement for the release of lanatoprost, an azetazolamide or pilocarpine derivative, dorzolamide, a **beta**-blocker, **alpha** - **agonist** or -antagonist, 5-fluorouracil, an antimetabolite, antiinfective, e.g. a virustatic, antibiotic or antimycotic, an antihistamine, steroid or antiinflammatory.

Extension Abstract:

EXAMPLE - None given in the source material.

Derwent Class: A96; B01; B05; B07; D22; P32; P34
International Patent Class (Main): A61F-002/14
International Patent Class (Additional): A61L-027/04; A61L-027/14

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     (FILE 'HOME' ENTERED AT 15:58:29 ON 30 JUN 2006)
     FILE 'REGISTRY' ENTERED AT 15:58:43 ON 30 JUN 2006
                E TETRACAINE/CN
L1            1 S E3
                E BRIMONIDINE/CN
L2            1 S E3
                E ALPHA 1 AGONIST
                E ALPHA-1 AGONIST/CN
                E ALPHA ADRENERGIC/CN
     FILE 'HCAPLUS' ENTERED AT 16:00:36 ON 30 JUN 2006
L3         2941 S L1 OR L2
L4        75526 S VASOCONSTRICT? OR VASOPRESS? OR VASOACTIVE OR ALPHA(1W)AGONIS
L5         3166 S TETRACAINE OR BRIMONIDINE
L6          365 S (L3 OR L5) AND L4
L7       411309 S ABSORB?
L8            4 S L6 AND L7 [not relevant]
L9       125938 S GLAUCOMA OR EYE OR OCULAR OR TRABECUL? OR ANTERIOR CHAMBER OR
L10           41 S L6 AND L9
L11      1292342 S 2004/PY
L12      1285812 S 2005/PY
L13       620212 S 2006/PY
L14           23 S L10 NOT (L11 OR L12 OR L13)
L15      1259587 S 2003/PY
L16            3 S L14 AND L15
L17           20 S L14 NOT L16
```

L16 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:814545 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 140:192973
TITLE: **Intraocular Pressure, Safety, and Quality of Life in ***Glaucoma*** Patients Switching to Latanoprost from Monotherapy Treatments**
AUTHOR(S): Zimmerman, Thom J.; Stewart, William C.
CORPORATE SOURCE: The Latanoprost Axis Study Group, University of Louisville, Louisville, KY, USA
SOURCE: Journal of **Ocular** Pharmacology and Therapeutics (***2003***), 19(5), 405-415
CODEN: JOPTFU; ISSN: 1080-7683
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose was to evaluate the efficacy, safety and quality of life in ***ocular*** hypertensive or open-angle ***glaucoma*** patients who required alteration in previous therapy and were changed to latanoprost. A prospective, multicenter, active, historical controlled trial in which qualified patients had previous therapy substituted with latanoprost 0.005% and were followed for up to 6 mo. 3179 Patients were included in the intent-to-treat anal. In all patients latanoprost reduced the intra**ocular** pressure (IOP) from 20.1.+-.3.9 to 17.1.+-.3.5 mm Hg (p< 0.0001) and when compared to previous monotherapies: **beta**-blockers (-3.0.+-.3.5, n = 1976), ***alpha*** - ***agonists*** (-3.6.+-.3.7, n = 581), miotics (-2.8.+-.3.0, n = 21), carbonic anhydrase inhibitors (-3.2.+-.3.5, n = 198), and other prostaglandin analogs (-1.6.+-.3.7, n = 402). The most common ***ocular*** adverse event with latanoprost was conjunctival hyperemia (n = 66, 2.0% incidence) and the most common

systemic adverse event was headache (n = 9, 0.2%). Over the 6-mo treatment interval 89.8% of patients were maintained on latanoprost. On the solicited symptom survey patients showed a preference for latanoprost compared to previous therapy for several reasons: (depending on the product) dryness, blurred vision, tearing, stinging on instillation, crusting, itching, fatigue, dizziness, despondency and dry mouth ($p < 0.005$). Latanoprost generally provides reduced IOP, limited side-effects, improvement in many quality of life measures and is maintained in patients who required a substitution from previous monotherapy.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:89237 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 139:270940
TITLE: *****Ocular*** Perfusion Pressure and Visual Field Indice Modifications Induced by . ***alpha*** .- ***Agonist*** Compound (Clonidine 0.125%, Apraclonidine 1.0% and ***Brimonidine*** 0.2%) Topical Administration**
AUTHOR(S): Costagliola, Ciro; Parmeggiani, Francesco; Ciancaglini, Marco; D'Oronzo, Emanuele; Mastropasqua, Leonardo; Sebastiani, Adolfo
CORPORATE SOURCE: **Eye** Clinic, University of Ferrara, Ferrara, I-44100, Italy
SOURCE: Ophthalmologica (***2003***), 217(1), 39-44
CODEN: OPHTAD; ISSN: 0030-3755
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of this study was to verify the acute effects of . *****alpha***** .-adrenoreceptor *****agonist***** **eye**drop administration on visual field parameters and *****ocular***** perfusion pressure (OPP) in patients affected by primary open-angle *****glaucoma***** . A prospective, randomized double-blind study was carried out. Sixty-four **glaucoma**tous subjects were enrolled in the clin. trial and subsequently sepd. into four study groups, of 16 patients each, to compare the systemic and *****ocular***** effects of placebo, clonidine 0.125%, apraclonidine 1.0% and *****brimonidine***** 0.2%. No significant variations in the *****ocular***** or systemic parameters were obsd. after placebo administration. All the . *****alpha***** .-adrenoreceptor *****agonist***** compds. induced a significant redn. of the intra**ocular** pressure. Clonidine induced significant modifications of mean blood pressure, OPP and visual field indexes. The acute administration of apraclonidine did not affect both mean blood pressure and OPP, but a worsening of the visual field was nevertheless recorded. **The analyzed parameters did not significantly vary after ***brimonidine*** instillation. The present findings demonstrate that the lack of effects on the blood flow and the absence of vasomotor activity at the level of the posterior pole exhibited by ***brimonidine*** is related to its .alpha.-2 selectivity, as appears by comparing this compd. with the other . ***alpha*** .- ***agonists*** available for the management of ***glaucoma*** .**

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:240512 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 136:284426
TITLE: Self-preserved nasal, inhalable, and topical ophthalmic preparations and medications
INVENTOR(S): Shahinian, Lee; Jr.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024116	A1	20020328	WO 2001-US29485	20010920
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2423354	AA	20020328	CA 2001-2423354	20010920
AU 2001091159	A5	20020402	AU 2001-91159	20010920
EP 1328214	A1	20030723	EP 2001-971254	20010920 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-234319P P 20000920
WO 2001-US29485 W 20010920

AB Self-preserved nasal, inhalable and topical ophthalmic prepns. and medications which destroy, inhibit or therapeutically significantly limit microbial growth within said prepns. or medications. The nasal, inhalable, and topical ophthalmic prepns. and medications are mildly buffered and maintain a stable pH at pH 3.5 or lower. An artificial tear contained polyethylene glycol-400 8, HPMC 0.3, citric acid 0.01, and water q.s. 100%.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:652234 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 136:63936
TITLE: Neuroprotective effect of . ***alpha* .2 ***agonist*** (***brimonidine***) on adult rat retinal ganglion cells after increased intraocular pressure**
AUTHOR(S): Ahmed, F. A. K. M.; Hegazy, K.; Chaudhary, P.; Sharma, S. C.
CORPORATE SOURCE: Department of Ophthalmology, New York Medical College, Valhalla, NY, 10595, USA
SOURCE: Brain Research (2001), 913(2), 133-139

CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ***Brimonidine*** , a selective .**alpha**.2-adrenoceptor **agonist**, has recently been shown to be neuroprotective as it significantly improves survival of retinal ganglion cells (RGCs) after calibrated optic nerve injury in rats. In the present study, we examd. the effect of ***brimonidine*** (.**alpha**.2-adrenoceptor **agonist**) on RGC survival after increased intra**ocular** pressure (IOP) in adult rats. RGCs were prelabeled by bilateral tectal injection of 5% Fluoro-Gold (FG). Two days later, unilaterally IOP was increased 2.2-2.5 times (28-30.5 mmHg) that of the normal pressure (12.5-14.5 mmHg) by cauterization of three episcleral veins. The elevated IOP was maintained throughout the duration of the expt. Rats were treated i.p. with ***brimonidine*** (1 mg/kg) or phosphate-buffered saline (PBS) once per wk beginning either before (group A) or after (group B) increasing the IOP. Another group of rats was left as the control with elevated IOP but without any ***brimonidine*** /PBS treatment. Rats were euthanized at 3, 4 and 5 wk after IOP elevation. Identifiable RGCs were counted and compared between control and exptl. groups. ***Brimonidine*** significantly protected RGCs from elevated IOP-induced cell death. In control rats with three-vein cauterization, there was 5-6% cell death per wk. Almost all RGCs were protected following ***brimonidine*** treatment for 3 wk both in groups A and B. At 4 wk, there was 4.5% cell death in group A and 6.5% in group B. At 5 wk, cell death was 5.9% in group A and 6.2% in group B. The difference in cell death in groups A and B was insignificant. No significant differences were obsd. between PBS-treated and control groups. No significant changes in elevated IOP was found after ***brimonidine*** or PBS treatment when compared with the nontreated control group. Although pressure remained elevated throughout the length of the expt., 3 wk later the amt. of cell death gradually increased in ***brimonidine*** -treated animals.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:501571 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 135:283115
TITLE: Differential effects of . ***alpha* .-adrenoceptor ***agonists*** on human retinal microvessel diameter**
AUTHOR(S): Spada, Clayton S.; Nieves, Amelia L.; Burke, James A.; Wheeler, Larry A.; Woodward, David F.
CORPORATE SOURCE: Department of Biological Sciences, Pharmaceutical Research & Development, Allergan, Inc., Irvine, CA, USA
SOURCE: Journal of **Ocular** Pharmacology and Therapeutics (2001), 17(3), 255-277
CODEN: JOPTFU; ISSN: 1080-7683
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of locally administered ***brimonidine*** , clonidine, and p-aminoclonidine on microvessel caliber were compared in human retinal tissues grafted into the hamster cheek pouch. Clonidine and

p-aminoclonidine, but not ***brimonidine*** , potently constricted human retinal microvessels over a broad concn. range. All three **agonists** elicited ***vasoconstriction*** in naive hamster cheek pouch microvasculature. The .**alpha**.2-adrenoceptor **antagonist** rauwolscine inhibited p-aminoclonidine-induced constriction in naive hamster cheek pouch microvessels, but not in retinal grafts. Selective .**alpha**.1-adrenoceptor **agonists** evoked ***vasoconstriction*** in retinal grafts only at relatively high concns. These differential effects on the retinal microvasculature could not be readily explained solely on the basis of .**alpha**.1- or .**alpha**.2-adrenoceptor involvement. Clonidine, p-aminoclonidine and ***brimonidine*** are also imidazoline derivs. that interact with putative nonadrenergic imidazoline-sensitive binding sites, the so-called I1-imidazoline binding site subtype implicated by some investigators in mediation of peripheral ***vasoconstriction*** . As with p-aminoclonidine, the potent ***vasoconstriction*** in human retinal microvasculature elicited by moxonidine, an . ***alpha*** .-adrenergic ***agonist*** that has also been reported to exhibit selectivity for putative I1-imidazoline binding sites, was not inhibited by the selective .**alpha**.-adrenoceptor **antagonist** rauwolscine, nor by idazoxan, an **antagonist** characterized as having substantial activity at putative I2-imidazoline binding sites. These data suggest the possible involvement of an unconventional nonadrenergic imidazoline-sensitive pathway in regulation of microvascular responses in the inner retina; drug activity mediated via such an imidazoline-sensitive component could potentially evoke deleterious effects in the retinal microvasculature.

REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:501565 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 135:251926
TITLE: **Effect of ***brimonidine*** tartrate on ***ocular*** hemodynamics in healthy volunteers**
AUTHOR(S): Jonescu-Cuypers, Christian P.; Harris, Alon; Ishii, Yoko; Kagemann, Larry; Gazozi, Hanna J.; Rotenstreich, Ygal; Chung, Hak Sung; Martin, Bruce
CORPORATE SOURCE: **Glaucoma** Research and Diagnostic Center, Department of Ophthalmology, Indiana University Medical Center, Indianapolis, IN, USA
SOURCE: Journal of **Ocular** Pharmacology and Therapeutics (2001), 17(3), 199-205
CODEN: JOPTFU; ISSN: 1080-7683
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB While .**alpha**.2-adrenergic **agonists**, such as ***brimonidine*** tartrate, significantly reduce the intra**ocular** pressure (IOP), the presence of ***vasoconstrictor*** postsynaptic .**alpha**.2 receptors on vascular smooth muscle raise the possibility that ***brimonidine*** could potentially compromise ***ocular*** blood flow. Consequently, the ***ocular*** hemodynamic effects of ***brimonidine*** were studied in normal subjects. Twelve healthy volunteers were included in this prospective, double-masked, placebo controlled, crossover-designed clin. trial. They received either ***brimonidine*** tartrate 0.2% or

placebo b.i.d. for 2 wk. Goldmann tonometry and color Doppler imaging (CDI) were performed at baseline, at 2 h, 1 wk, and 2 wk after the treatment. Fundus angiog. using a scanning laser ophthalmoscope was performed at baseline and 2 wk after treatment to det. retinal arteriovenous passage time. ***Brimonidine*** lowered IOP at 2 h, 1 wk, and 2 wk ($p = 0.058$, $p = 0.031$, and $p = 0.022$, resp.). ***Brimonidine*** did not affect the retrobulbar arterial velocities measured by CDI, nor retinal arteriovenous passage time. In conclusion, two-week treatment with ***brimonidine*** reduces IOP and does not reduce the bulk retinal or retrobulbar arterial perfusion in young healthy volunteers.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:402581 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 135:251913
TITLE: **Efficacy of ***brimonidine*** 0.2% and dorzolamide 2% as adjunctive therapy to beta-blockers in adult patients with ***glaucoma*** or ***ocular*** hypertension**
AUTHOR(S): Simmons, Steven T.
CORPORATE SOURCE: **Glaucoma** Consultants of the Capital Region, Slingerlands, NY, USA
SOURCE: Clinical Therapeutics (2001), 23(4), 604-619
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: The ***alpha*** -adrenergic ***agonist*** ***brimonidine*** and the carbonic anhydrase inhibitor dorzolamide have been studied both as monotherapy and in combination with **beta**-blockers in the treatment of ***glaucoma*** and ***ocular*** hypertension; however, a MEDLINE literature search failed to reveal any clin. studies directly comparing these 2 agents as adjunctive therapy. Objective: The purpose of this study was to compare the intra**ocular** pressure (IOP)-lowering efficacy of ***brimonidine*** and dorzolamide as adjunctive therapy to **beta**-blockers in adult patients with ***glaucoma*** or ***ocular*** hypertension. Methods: In a prospective, investigator-masked, multicenter, parallel-design clin. trial, adult patients whose IOP was inadequately controlled with topical **beta**-blocker therapy were randomly assigned to receive ***brimonidine*** 0.2% twice daily or dorzolamide 2% 3 times daily as adjunctive therapy for 3 mo. Efficacy was detd. by the redn. in IOP from baseline. After 1 mo of adjunctive treatment, patients who failed to meet a target 15% redn. in IOP at peak drug effect were crossed over to the other study medication. Results: A total of 106 patients were treated. Approx. 70% (74/106) of the patients were white, and 61.3% (65/106) had a diagnosis of open-angle ***glaucoma*** . Mean baseline IOP (ie, with **beta**-blocker monotherapy) was comparable between treatment groups (.apprx.21 mm Hg). After 1 mo of adjunctive treatment, the mean daily IOP redn. was significantly greater with ***brimonidine*** (4.40 mm Hg, 20.4%) than with dorzolamide (3.0 mm Hg, 14.4%; P = 0.033). At peak drug effect at month 1, the mean IOP redn. was significantly greater in the ***brimonidine*** group (5.95 mm Hg, 27.6%) than in the dorzolamide group (4.11 mm Hg, 19.7%; P =

0.007). Significantly more patients treated with ***brimonidine*** (44/51, 86.3%) than with dorzolamide (29/47, 61.7%) achieved the target 15% redn. in IOP at month 1 (P = 0.005). At month 3, the mean daily IOP redn. and the mean IOP redn. at peak drug effect were not significantly different in the 2 treatment groups. The mean daily IOP redn. was 4.98 mm Hg in the ***brimonidine*** group and 3.15 mm Hg in the dorzolamide group (P = 0.092). At peak drug effect, the mean IOP redn. was 6.39 mm Hg with ***brimonidine*** and 4.06 mm Hg with dorzolamide. The incidence of adverse events leading to discontinuation was 9.3% (5/54) in the ***brimonidine*** group (depression, 2; allergic conjunctivitis, 1; dry mouth and tearing, 1; dermatitis, 1) and 9.8% (5/51) in the dorzolamide group (***ocular*** burning and stinging, 2; ***ocular*** itch, 1; gastrointestinal complaints, 1; lack of tolerance for **beta**-blocker, 1), with no significant difference between groups. Conclusion: In this trial, ***brimonidine*** 0.2% twice daily produced greater mean decreases in IOP and was effective in more patients than dorzolamide 2% 3 times daily when used as adjunctive therapy to **beta**-blockers.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:250752 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 132:246141
TITLE: **The effect of ***brimonidine*** tartrate on retinal blood flow in patients with ***ocular*** hypertension**
AUTHOR(S): Carlsson, Anthony M.; Chauhan, Balwantray C.; Lee, A. Arlene; LeBlanc, Raymond P.
CORPORATE SOURCE: Faculty of Medicine, Dalhousie University, Halifax, NS, B3H 2Y9, Can.
SOURCE: American Journal of Ophthalmology (2000), 129(3), 297-301
CODEN: AJOPAA; ISSN: 0002-9394
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PURPOSE: To study the effects of topical ***brimonidine*** tartrate 0.2%, an . ***alpha*** .2- ***agonist*** ***ocular*** hypotensive drug, on retinal capillary blood flow in patients with ***ocular*** hypertension. METHODS: The study was a double-masked, randomized, placebo-controlled trial set in a tertiary ***eye*** center. ***Ocular*** hypertensive patients with repeatable intra**ocular** pressures greater than 21 mm Hg and normal visual fields and optic disks were consecutively recruited. After an ***eye*** examn., baseline retinal blood flow measurements were made with confocal scanning laser Doppler flowmetry in one study ***eye*** . Patients were then randomly assigned to receive either ***brimonidine*** or placebo (saline) twice daily for 8 wk. Blood flow and intra**ocular** pressure measurements were then repeated after 4 and 8 wk. RESULTS: Seventeen patients were randomly assigned to receive ***brimonidine*** , and 14 received placebo. One patient in each group failed to complete the study. The mean group differences in baseline age and intra**ocular** pressure were not statistically significant (59.23 [.+-. 10.24] and 52.23 [.+-. 16.46] years, resp., and 24.84 [.+-. 2.08] and 24.56 [.+-. 2.85] mm Hg, resp.). ***Brimonidine*** reduced intra**ocular** pressure by 17.90% and 16.17% at 4

and 8 wk, resp., with a significant difference in treatment effect compared with the placebo group (P <.007). The group difference in treatment effect in any of the three hemodynamic parameters velocity, vol., and flow was within 8% and not significantly different at 4 or 8 wk (P >.360). Based on a type I error of 0.05, our study had a power greater than or equal to 75% to detect group differences in treatment effect of greater than or equal to 15% to 20%. CONCLUSIONS: ***Brimonidine*** reduces intra**ocular** pressure without altering retinal capillary blood flow in patients with ***ocular*** hypertension.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:517687 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 131:165138
TITLE: **The short-term effect of adding ***brimonidine*** 0.2% to timolol treatment in patients with open-angle ***glaucoma***
AUTHOR(S): Yuksel, Nursen; Altintas, Ozgul; Karabas, Levent; Alp, Banu; Caglar, Yusuf
CORPORATE SOURCE: Department of Ophthalmology, School of Medicine, Kocaeli University, Kocaeli, Turk.
SOURCE: Ophthalmologica (1999), 213(4), 228-233
CODEN: OPHTAD; ISSN: 0030-3755
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ***Brimonidine*** , a highly selective .**alpha**.2-adrenoceptor **agonist**, was studied to det. its ***ocular*** hypotensive effect and side effects in patients with elevated intra**ocular** pressure (IOP) while on continuing therapy with timolol. This was a prospective, randomized, placebo-controlled study in 15 patients with primary open-angle or pseudoexfoliation ***glaucoma*** on therapy receiving timolol 0.5% twice daily, with IOP greater than or equal to 22 mm Hg in one ***eye*** . IOP measurements, blood pressure and pulse rate were assessed on 2 days at a baseline and 1, 2, 4, 6 and 8 h later. A single drop of ***brimonidine*** 0.2% or placebo was added to treatment with timolol. The redns. in IOP at all time intervals obsd. with ***brimonidine*** + timolol were significantly greater than those with timolol + placebo. The max. mean net decrease in IOP was 19.23.+-.10.60% at 4 h. Statistically significant decreases in systemic blood pressure and pulse rate without clin. symptoms were obsd. in the group receiving ***brimonidine*** + timolol. This study suggests that a combination of ***brimonidine*** and timolol may have potential in the treatment of ***glaucoma*** . Further clin. trials with ***brimonidine*** are indicated to assess its further role as adjunctive agent.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:482543 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 129:169985
TITLE: **Changing therapeutic paradigms in ***glaucoma*** management**

AUTHOR(S): David, Robert
CORPORATE SOURCE: Allergan, Irvine, CA, USA
SOURCE: Expert Opinion on Investigational Drugs (1998), 7(7), 1063-1086
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 215 refs. ***Glaucoma*** is a family of diseases commonly characterized by progressive optic neuropathy with assocd. visual field deficits for which elevated intra**ocular** pressure (IOP) is one of the primary risk factors. For more than a century the main goal of ***glaucoma*** management has been to eliminate the risk assocd. with elevated IOP. In recent years, accumulating evidence of pressure-independent causes of **glaucoma**tous optic neuropathy has led to the recognition that lowering IOP alone may often be insufficient for the long-term preservation of visual function. An innovative therapeutic approach is now emerging to prevent progression of **glaucoma**tous optic neuropathy and preserve vision, irresp. of disease etiol.: direct protection of the optic nerve. In addn. to reducing the risk assocd. with elevated IOP, this neuroprotective approach will augment the overall goal of preserving the optic nerve through direct promotion of retinal ganglion cell (RGC) survival and/or prevention of RGC death. Although no currently available compds. have been clin. demonstrated to provide neuroprotective benefit in ***glaucoma*** , recent preclin. studies have shown that . ***alpha*** .-adrenergic ***agonists*** , such as ***brimonidine*** , provide neuroprotective benefits, as well as excellent IOP-lowering efficacy. In addn., new agents with promising neuroprotective utility that are emerging from other studies are now being investigated for efficacy in ***glaucoma*** . This review discusses recently introduced compds. and new drugs in development with regard to their potential value in conventional and/or neuroprotective strategies for vision sparing in ***glaucoma*** .

REFERENCE COUNT: 218 THERE ARE 218 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:298380 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 128:289652
TITLE: .alpha.-Adrenergic drugs
AUTHOR(S): Kuwayama, Yasuaki
CORPORATE SOURCE: Dep. Ophthalmol., Osaka Koseinenkin Hosp., Osaka, 553-0003, Japan
SOURCE: Atarashii Ganka (1998), 15(4), 463-468
CODEN: ATGAEX; ISSN: 0910-1810
PUBLISHER: Medikaru Ai Shuppan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 25 refs., on the therapeutic use of .**alpha**.1-**antagonists** and . ***alpha*** .2- ***agonists*** in the treatment of ***glaucoma*** . Effects of bunazosin hydrochloride, apraclonidine hydrochloride, and ***brimonidine*** on the intra**ocular** pressure and blood flow, and clin. efficacy, adverse effects, and future prospects of these drugs are discussed. **Subclasses of .alpha.-receptors and signal transduction**

pathways mediated by .alpha.1- and .alpha.2- receptors are also described.

L17 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:525320 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 127:171565
TITLE: **A 1-year study of ***brimonidine*** twice daily in ***glaucoma*** and ***ocular*** hypertension: a controlled, randomized, multicenter clinical trial**
AUTHOR(S): Schuman, Joel S.; Horwitz, Barry; Choplin, Neil T.; David, Robert; Albracht, Diane; Chen, Kuankuan
CORPORATE SOURCE: The Chronic **Brimonidine** Study Group, New England **Eye** Center, Tufts University School of Medicine, Boston, MA, USA
SOURCE: Archives of Ophthalmology (Chicago) (1997), 115(7), 847-852
CODEN: AROPAW; ISSN: 0003-9950
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ***Brimonidine*** tartrate is a highly selective . ***alpha*** .2-***agonist*** . This study investigates the safety and efficacy of 0.2% ***brimonidine*** administered twice daily for 1 yr in patients with ***glaucoma*** or ***ocular*** hypertension. The study design was a multicenter, double-masked, randomized, parallel-group, active-controlled comparison clin. trial. Subjects instilled 0.2% ***brimonidine*** or 0.5% timolol maleate twice daily for 12 mo. Subjects were examd. at baseline, week 1, and months 1, 2, 3, 6, 9, and 12. A subset of subjects was examd. at week 2. Of 443 subjects enrolled in this study, 374 met the entry criteria; 186 received ***brimonidine*** and 188 received timolol. ***Brimonidine*** -treated subjects showed an overall mean peak redn. in intra**ocular** pressure (IOP) of 6.5 mm Hg; timolol-treated subjects had a mean peak redn. in IOP of 6.1 mm Hg. ***Brimonidine*** lowered mean peak IOP significantly more than timolol at week 2 and month 3 (P<.03); no significant difference was obsd. between the groups for this variable at other visits throughout the 1-yr course of the study. No evidence of tachyphylaxis was seen in either group. Allergy was seen in 9% of subjects treated with ***brimonidine*** . Dry mouth was more common in the ***brimonidine*** -treated group than in the timolol-treated group (33.0% vs 19.4%), but complaints of burning and stinging were more common in the timolol-treated group (41.9%) than in the ***brimonidine*** -treated patients (28.1%). Headache, fatigue, and drowsiness were similar in the 2 groups. In general, the tolerance to medication was acceptable. ***Brimonidine*** is safe and effective in lowering IOP in **glaucoma**tous **eyes**. ***Brimonidine*** provides a sustained long-term ***ocular*** hypotensive effect, is well tolerated, and has a low rate of allergic response.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:107455 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 126:122452
TITLE: **Compositions and methods for topical administration of pharmaceutically active agents**

INVENTOR(S): Kanios, David P.; Gentile, Joseph A.; Mantelle, Juan A.; Sablotsky, Steven
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., USA; Kanios, David P.; Gentile, Joseph A.; Mantelle, Juan A.; Sablotsky, Steven
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640086	A2	19961219	WO 1996-US8294	19960605
WO 9640086	A3	19970213		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9526998	A1	19961230	AU 1995-26998	19950607
US 5719197	A	19980217	US 1995-477361	19950607
AU 9660290	A1	19961230	AU 1996-60290	19960605
PRIORITY APPLN. INFO.:			US 1995-477361 A	19950607
			US 1988-164482 A2	19880304
			US 1989-295847 A2	19890111
			US 1991-661827 B2	19910227
			US 1991-671709 A1	19910402
			US 1991-813196 A2	19911223
			US 1993-67001 A2	19930526
			US 1993-112330 A2	19930827
			WO 1995-US7229 W	19950607
			WO 1996-US8294 W	19960605

AB Compns. for topical application comprising a therapeutically effective amt. of a pharmaceutical agent(s), a pharmaceutically acceptable bioadhesive carrier, a solvent for the pharmaceutical agent(s) in the carrier and a clay, and methods of administering the pharmaceutical agents to a mammal are disclosed. Thus, a formulation of the invention can be prepd. which consists (wt. %) of lidocaine base 8.0, dipropylene glycol 5.0, 60% lecithin in propylene glycol 8.0, bentonite (Polargel NF) 2.0, zinc oxide 0.1, and glycerin 6.0.

L17 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:654595 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 125:298660
TITLE: Contractile response of the isolated ***trabecular* meshwork and ciliary muscle to cholinergic and adrenergic agents**
AUTHOR(S): Wiederholt, Michael; Schaefer, Roland; Wagner, Ulrike; Lepple-Wienhues, Albrecht
CORPORATE SOURCE: Institut fur Klinische Physiologie, Freie Universitat Berlin, Berlin, D-12200, Germany
SOURCE: German Journal of Ophthalmology (1996), 5(3), 146-153
CODEN: GJOPEC; ISSN: 0941-2921

PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To characterize the contractile properties of isolated ***trabecular*** meshwork strips, we measured the effect of various cholinergic and adrenergic substances on the contractility of ***trabecular*** meshwork (TM) strips in comparison with the effects on ciliary muscle (CM) strips. Using an electromagnetic force-length transducer, we performed measurements of isometric tension on isolated bovine TM and CM strips. Isolated strips were contracted by cholinergic **agonists**, the relative potency being carbachol > pilocarpine > acetylcholine. The half-maximal effective concn. was 2.times.10-7 mol l-1 for carbachol and 2.times.10-6 mol l-1 for pilocarpine. To characterize muscarinic receptors, we tested selective **antagonists** for M1 (pirenzepine) and M3 (4-DAMP). Pharmacol., the functional muscarinic receptors are of the M3 subtype in TM as well as CM. The M1 subtype seems to be less important. The . ***alpha*** .1- ***agonist*** phenylephrine was more effective in inducing contractions in TM than in CM. The . ***alpha*** .2- ***agonist*** ***brimonidine*** induced contractions only in TM. In precontracted tissues the .**beta**.-**agonist** isoproterenol induced a relaxation in both tissues. This relaxation could be inhibited by metipranolol. Epinephrine (or dipivefrin) induced small contractions in TM and CM, which became more prominent, esp. in TM, when the .**beta**.-adrenoreceptors were inhibited by metipranolol. The data indicate the presence of functional muscarinic, .**alpha**.-adrenergic, and .**beta**.-adrenergic receptors in bovine TM and CM. The contractile properties of TM and CM are differently modulated by the various drugs. Cholinergic and . ***alpha*** .-adrenergic ***agonists*** induced contraction, whereas .**beta**.-**agonists** induced relaxation.

L17 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:220267 HCAPLUS <<LOGINID::20060630>>
TITLE: **Synthesis and characterization of degradation products and metabolites of ***brimonidine*** - A potent .alpha.2 adrenergic agonist.**
AUTHOR(S): Munk, S. A.; Harcourt, D.; Wong, H.; Acheampong, A.; Breau, A.; Tang-Liu, D.; Burke, J.; Lai, R.; Wheeler, L.; Garst, M.
CORPORATE SOURCE: Allergan Pharmaceuticals, Irvine, CA, 92715, USA
SOURCE: Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), MEDI-021. American Chemical Society: Washington, D. C.
CODEN: 62PIAJ
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB ***Brimonidine*** (UK 14,304; AGN 190342) is currently being evaluated as a topical ***ocular*** antihypertensive. Elevated intra**ocular** pressure is a symptom often assocd. with ***glaucoma*** , a leading cause of blindness. Herein, we detail the syntheses of putative metabolites and degrdn. products of ***Brimonidine*** . These agents were confirmed as metabolites and degrdn. products both spectroscopically and chromatog. The compds. proved to be less potent as . ***alpha*** .2 ***agonists*** than ***Brimonidine*** .

L17 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:480248 HCAPLUS <<LOGINID::20060630>>
DOCUMENT NUMBER: 119:80248
TITLE: **Combination of selective ***alpha*** -adrenergic ***agonists*** and Na+/H+ exchange inhibitors for lowering intraocular pressure**
INVENTOR(S): Burke, James A.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S., 12 pp. Cont. of U.S. Ser. No. 470,848, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5215991	A	19930601	US 1990-633103	19901220
PRIORITY APPLN. INFO.:			US 1990-470848	B1 19900126

AB Combination of selective ***alpha*** -adrenergic ***agonists*** and Na+/H+ exchange inhibitors are used for lowering intraocular pressure (IOP). Administration of 5-(N,N-hexamethylene)amiloride resulted in .DELTA.IOP of +2.6 while coadministration with p-aminoclonidine (30min later) resulted in .DELTA.IOP -7.5mmHg after 3h.

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File 350:Derwent WPIX 1963-2006/UD,UM &UP=200641
         (c) 2006 The Thomson Corp.
File 349:PCT FULLTEXT 1979-2006/UB=20060622,UT=20060615
         (c) 2006 WIPO/Univentio
File 348:EUROPEAN PATENTS 1978-2006/ 200626
         (c) 2006 European Patent Office
Set     Items   Description
S1        307   AU='TU H' OR AU='TU HOSHENG' OR AU='TU HOSHENG (ROGER)' OR
              AU='TU HOSHENG ROGER'
S2      13544   VASOMODULAT? OR VASOCONSTRICT? OR ALPHA(1W)AGONIST? OR TET-
              RACAINE OR BRIMONIDINE OR BETA()ADRENERGIC()ANTAGONIST?
S3         10   S1 AND S2

3/3,AB,IC/1     (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2006 The Thomson Corp. All rts. reserv.
017890485
WPI Acc No: 2006-401801/200641
Related WPI Acc No: 2004-327166
XRAM Acc No: C06-127689
XRPX Acc No: N06-334886
Treatment glaucoma comprises inserting outflow element through incision in eye,
introducing outflow portion through trabecular meshwork into aqueous cavity and
infusing fluid from delivery element through delivery lumen
Patent Assignee: HAFFNER D (HAFF-I); SMEDLEY G (SMED-I); TU H (TUHH-I)
Inventor: HAFFNER D; SMEDLEY G;  TU H
Number of Countries: 001  Number of Patents: 001
Patent Family:
Patent No     Kind   Date    Applicat No    Kind   Date     Week
US 20060116626  A1  20060601  US 2002362405   P   20020307  200641  B
                            US 2002363980   P   20020314
                            US 2003384912   A   20030307
                            US 2006332746   A   20060112
Priority Applications (No Type Date): US 2006332746 A 20060112; US
  2002362405 P 20020307; US 2002363980 P 20020314; US 2003384912 A 20030307
Patent Details:
Patent No  Kind Lan Pg   Main IPC    Filing Notes
US 20060116626 A1    15 A61M-005/00   Provisional application US 2002362405
                                      Provisional application US 2002363980
                                      Cont of application US 2003384912
Abstract (Basic): US 20060116626 A1
Abstract (Basic):
        NOVELTY - Treating glaucoma comprises inserting outflow element
    through incision in eye having aqueous cavity, advancing the outflow
    portion through the trabecular meshwork into the aqueous cavity,
    positioning the outflow element in the aqueous cavity, providing a
    delivery element having a delivery lumen and infusing fluid through the
    delivery lumen to the outflow element lumen.
        DETAILED DESCRIPTION - Treatment of glaucoma comprises inserting an
    outflow element through an incision in an eye having an aqueous cavity,
    transporting the outflow portion through the anterior chamber from the
    incision to the trabecular meshwork, advancing the outflow portion
    through the trabecular meshwork into the aqueous cavity of the eye,
    positioning the outflow element in the aqueous cavity, providing a
    delivery element having a delivery lumen, coupling the delivery element
    to the outflow element and infusing fluid through the delivery lumen to
```

the outflow element lumen.

The outflow element has an inflow portion in fluid communication through an outflow element lumen with an outflow portion of the outflow element. The fluid flows from the inflow portion to the outflow portion and into the aqueous cavity selected from Schlemm's canal, aqueous collector channel, or episcleral vein of eye.

ACTIVITY - Ophthalmological.

No biological data is given.

MECHANISM OF ACTION - None given.

USE - Used for treating glaucoma.

pp; 15 DwgNo 0/6

International Patent Class (Main): A61M-005/00

3/3,AB,IC/2 (Item 2 from file: 350)

DIALOG(R)File 350:Derwent WPIX

017375762

WPI Acc No: 2005-699411/200572

XRAM Acc No: C05-212732

Use of a compound of topiramate having glutamate receptor inhibitory activity, to treat macular degeneration and to treat or prevent optic neuropathy

Patent Assignee: CHU P (CHUP-I); TU H (TUHH-I)

Inventor: CHU P; **TU H**

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
US 6949518	B1	20050927	US 2003482585	P	20030625	200572	B
			US 2004868731	A	20040615		

Priority Applications (No Type Date): US 2003482585 P 20030625; US 2004868731 A 20040615

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 6949518	B1		7	A61K-031/70	Provisional application US 2003482585

Abstract (Basic): US 6949518 B1

Abstract (Basic):

NOVELTY - Treatment of macular degeneration in a subject comprises administering a compound (I) of topiramate or its analogs, isomers or derivatives.

ACTIVITY - Ophthalmological; Neuroprotective; Analgesic.

MECHANISM OF ACTION - Sodium channel blocker; Gamma aminobutyric acid-a receptor enhancer; Glutamate receptor inhibitor; L-Type high-voltage calcium ion channel inhibitor.

USE - (I) is useful to treat macular degeneration (claimed) and optic neuropathy. (I) is useful to treat or prevent optic nerve degeneration and to relieve neuropathic pain. No biological data given.

ADVANTAGE - (I) effectively lowers lipids in humans, particularly in overweight individuals. (I) improves both symptoms and objective electrophysiological measurements of peripheral neuropathy; lowers the level of total cholesterol, triglyceride, blood glucose, and blood pressure; and promotes significant weight loss. (I) reduces optic nerve degeneration and/or induces the growth of optic nerve fibers and/or stimulates the functions of optic nerves.

pp; 7 DwgNo 0/0

International Patent Class (Main): A61K-031/70

3/3,AB,IC/3 (Item 3 from file: 350)
DIALOG(R)File 350:Derwent WPIX

016635611
WPI Acc No: 2004-794324/200478
XRAM Acc No: C04-277144
XRPX Acc No: N04-626018
Minimization of blood reflux from episcleral vein or reduction of pain during glaucoma surgery, involves administering** vasoconstrictive **agent to eye of mammal to reduce blood flow through episcleral vein or reduce pain
Patent Assignee: TU H (TUHH-I)
Inventor: **TU H**
Number of Countries: 001 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 20040216749	A1	20041104	US 2003442098	P	20030123	200478 B
			US 2004763569	A	20040123	

Priority Applications (No Type Date): US 2003442098 P 20030123; US 2004763569 A 20040123
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 20040216749	A1		8	A61F-009/007	Provisional application US 2003442098

Abstract (Basic): US 20040216749 A1
Abstract (Basic):
NOVELTY - Minimization of blood reflux from an episcleral vein or reduction of pain during glaucoma surgery comprises placing a glaucoma implant into an eye of a mammal, and administering a **vasoconstrictive** agent to the eye to reduce blood flow through the episcleral vein or reduce pain.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method of enhancing penetration of a poorly absorbing eye medicine, comprising co-administering to the eye of a mammal a **vasoconstrictor** and poorly absorbing eye medicine.
ACTIVITY - Ophthalmological.
MECHANISM OF ACTION - **alpha** -Adrenergic **Agonist** ; **beta** -**Adrenergic antagonist**
USE - For minimizing blood reflux from an episcleral vein or reducing pain during glaucoma surgery.
ADVANTAGE - The method is faster, safer and less expensive.
pp; 8 DwgNo 0/0
International Patent Class (Main): A61F-009/007

3/3,AB,IC/5 (Item 1 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

01210292
DEVICES AND METHODS FOR GLAUCOMA TREATMENT
DISPOSITIFS ET METHODES DE TRAITEMENT DE GLAUCOMES
Patent Applicant/Assignee:
GLAUKOS CORPORATION, 26061 Merit Circle, Suite 101, Laguna Hills, CA 92653, US, US (Residence), US (Nationality), (For all designated states except: US)
Patent Applicant/Inventor:
HAFFNER David, 24681 Via San Fernando, Mission Viejo, CA 92692, US, US

(Residence), US (Nationality), (Designated only for: US)
SMEDLEY Gregory T, 15 Crimson Canyon, Akliso Viejo, CA 92650, US, US (Residence), US (Nationality), (Designated only for: US)
TU Hosheng , 15 Riez, Newport Beach, CA 92657, US, US (Residence), US (Nationality), (Designated only for: US
Legal Representative:
DELANEY Karoline A (agent), 2040 Main Street, Fourteenth Floor, Irvine, CA 92614, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200516418 A1 20050224 (WO 0516418)
Application: WO 2004US24988 20040803 (PCT/WO US04024988)
Priority Application: US 2003634213 20030805
Designated States:
(All protection types applied unless otherwise stated - for applications 2004+)
AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
(EP) AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU MC NL PL PT RO SE SI SK TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class (v7): A61M-005/00
Publication Language: English
Filing Language: English
Fulltext Word Count: 24349
English Abstract
Intraocular stents (229) and applicators are disclosed for treating glaucoma. **The stents (229) are configured to extend between the anterior chamber of the eye and Schlemm's canal** (22) for enhancing outflow of aqueous from the anterior chamber (20) so as to reduce intraocular pressure. The stents (229) can have features for anchoring the stent into Schlemm's canal (22) as well as preventing the walls of Schlemm's canal (22) from closing the outlet of the stents (229). The applicators can be steerable so as to make implantation easier. Additionally, the applicators can be configured to hold a plurality of stents so that multiple stents can be implanted through one incision without removing the applicator from the incision between serial implantations.

3/3,AB,IC/6 (Item 2 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00968586
GLAUCOMA DEVICE AND METHODS THEREOF
DISPOSITIF PERMETTANT DE TRAITER LE GLAUCOME ET METHODES ASSOCIEES
Patent Applicant/Assignee:
GLAUKOS CORPORATION, 26061 Merit Circle, Suite 101, Laguna Hills, CA 92653, US, US (Residence), US (Nationality)
Inventor(s):
BERGHEIM Olav, 2772 Deputy Circle, Laguna Hills, CA 92653, US,
TU Hosheng , 15 Riez, Newport Coast, CA 92657, US,
GHARIB Morteza, 556 South Berkeley Avenue, San Marino, CA 91108, US
Legal Representative:

ARAI Katsuhiro (agent), KNOBBE, MARTENS, OLSON & BEAR, LLP, 620 Newport Center Drive, 16th Floor, Newport Beach, CA 92660, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 2002102274 A2-A3 20021227 (WO 02102274)
Application: WO 2002US13872 20020501 (PCT/WO US0213872)
Priority Application: US 2001287902 20010501
Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)
AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ (utility model) CZ DE (utility model) DE DK (utility model) DK DM DZ EC EE (utility model) EE ES FI (utility model) FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK (utility model) SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class (v7): A61M-005/00
International Patent Class (v7): A61M-027/00
Publication Language: English
Filing Language: English
Fulltext Word Count: 12003
English Abstract
A glaucoma treatment device (31, 61) for directing the flow of aqueous humor and reducing intraocular pressure for angle closure glaucoma is disclosed. The glaucoma device (31, 61) comprises an aqueous transporting element (31, 61) for transporting aqueous humor to bypass dysfunctional anatomical iris closure and restoring existing outflow pathways of the anatomical iris closure. The aqueous transporting element (31, 61) has an inlet end (34, 90) and an outlet end (35, 92), wherein the inlet end (34, 90) is positioned inside an anterior chamber (20) of an eye (10) beyond an edge (120) of the dysfunctional anatomic iris closure and the outlet end (35, 92) is positioned in proximity of trabecular meshwork (21) of the eye (10). The device (31, 61) also serves to stent the space between the iris (13) and an inner surface (126) of a cornea (12) of the eye (10).

3/3,AB,IC/7 (Item 3 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00956015
MEDICAL DEVICE AND METHODS OF USE FOR GLAUCOMA TREATMENT
DISPOSITIF MEDICAL ET METHODES D'UTILISATION POUR LE TRAITEMENT D'UN GLAUCOME
Patent Applicant/Assignee:
GLAUKOS CORPORATION, Suite 101, 26061 Merit Circle, Laguna Hills, CA 92653, US, US (Residence), US (Nationality)
Inventor(s):
TU Hosheng , 15 Riez, Newport Coast, CA 92657, US,
SMEDLEY Gregory T, 81 Whitman Court, Irvine, CA 92612, US,
NIKSCH Barbara, 28571 Jaeger Drive, Laguna Niguel, CA 92677, US,
HAFFNER David S, 24681 Via San Fernando, Mission Viejo, CA 92692, US
Legal Representative:
ALTMAN Daniel E (agent), Knobbe, Martens, Olson & Bear, LLP, 16th Floor,

620 Newport Center Drive, Newport Beach, CA 92660, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200289699 A2-A3 20021114 (WO 0289699)
Application: WO 2002US14230 20020503 (PCT/WO US0214230)
Priority Application: US 2001288325 20010503
Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)
AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ (utility model) CZ DE (utility model) DE DK (utility model) DK DM DZ EC EE (utility model) EE ES FI (utility model) FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK (utility model) SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class (v7): A61M-029/00
Publication Language: English
Filing Language: English
Fulltext Word Count: 11307
English Abstract
The invention relates generally medical devices and methods for the treatment of glaucoma in an animal eye (10) and, more particularly, to medical devices and methods for treating tissue of the trabecular meshwork (21) and /or Schlemm's canal (22) of the eye (10) to restore or rejuvenate a portion or all of the normal physiological function of directing aqueous outflow for maintaining a normal intraocular pressure in the eye (10).

3/3,AB,IC/8 (Item 4 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00947130
GLAUCOMA STENT AND METHODS THEREOF FOR GLAUCOMA TREATMENT
STENT DE GLAUCOME ET PROCEDES DESTINES AU TRAITEMENT D'UN GLAUCOME
Patent Applicant/Assignee:
GLAUKOS CORPORATION, 26061 Merit Circle, Suite 101, Laguna Hills, CA 92653, US, US (Residence), US (Nationality)
Inventor(s):
TU Hosheng , 15 Riez, Newport Coast, CA 92657, US,
SMEDLEY Gregory T, Irvine, CA, US,
HAFFNER David S, Mission Viejo, CA, US,
NIKSCH Barbara A, Aliso Viejo, CA, US
Legal Representative:
ALTMAN Daniel E (agent), 2040 Main Street, Fourteenth Floor, Irvine, CA 92614, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200280811 A2-A3 20021017 (WO 0280811)
Application: WO 2002US11219 20020408 (PCT/WO US02011219)
Priority Application: US 2001281973 20010407
Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ (utility model) CZ DE (utility model) DE DK (utility model) DK DM DZ EC EE (utility model) EE ES FI (utility model) FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK (utility model) SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
(OA) BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class (v7): A61M-005/00
International Patent Class (v7): A61M-035/00
Publication Language: English
Filing Language: English
Fulltext Word Count: 14475
English Abstract

The invention relates generally to medical devices and methods for reducing the intraocular pressure in an animal eye (10) and, more particularly, to stent type devices (30) for permitting aqueous outflow from the eye's anterior chamber (20) and associated methods thereof for the treatment of glaucoma. Some aspects provide a self-trephining glaucoma stent (30) and methods thereof which advantageously allow for a "one-step" procedure in which the incision and placement of the stent (30) are accomplished by a single device and operation. This desirably allows for a faster, safer, and less expensive surgical procedure.

3/3,AB,IC/9 (Item 5 from file: 349)
DIALOG(R)File 349:PCT FULLTEXT

00902387
GLAUCOMA TREATMENT DEVICE
DISPOSITIF DE TRAITEMENT DU GLAUCOME
Patent Applicant/Assignee:
GLAUKOS CORPORATION, 26061 Merit Circle, #101, Laguna Hills, CA 92653, US , US (Residence), US (Nationality)
Inventor(s):
TU Hosheng (Roger) , 2151 Palermo, Tustin, CA 92782, US,
BERGHEIM Olav, 27722 Deputy Circle, Laguna Hills, CA 92653, US,
GHARIB Morteza, 556 South Berkeley Avenue, San Marino, CA 91108, US
Legal Representative:
ALTMAN Daniel E (agent), KNOBBE, MARTENS, OLSON & BEAR, LLP, 620 Newport Center Drive, 16th Floor, Newport Beach, CA 92660, US,
Patent and Priority Information (Country, Number, Date):
Patent: WO 200236052 A1 20020510 (WO 0236052)
Application: WO 2001US14783 20010508 (PCT/WO US0114783)
Priority Application: US 2000704276 20001101
Designated States:
(Protection type is "patent" unless otherwise stated - for applications prior to 2004)
AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ CZ (utility model) DE DE (utility model) DK DK (utility model) DM DZ EE EE (utility model) ES FI FI (utility model) GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SK (utility model) SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
(EP) AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

(OA) BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG
(AP) GH GM KE LS MW MZ SD SL SZ TZ UG ZW
(EA) AM AZ BY KG KZ MD RU TJ TM
Main International Patent Class (v7): A61F-009/007
Publication Language: English
Filing Language: English
Fulltext Word Count: 6968
English Abstract

A glaucoma treatment device for directing the flow of aqueous humor and bypassing trabecular meshwork is disclosed. The device comprises an inlet section, an outlet section, a middle section, and at least one lumen for transmitting aqueous humor within the glaucoma device. The lumen extends through at least one of the sections, and the outlet section is substantially perpendicular to the middle section and fits within a conduit of aqueous humor outflow in the eye.

3/3,AB,IC/10 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01578661
Drug-releasing trabecular implant for glaucoma treatment
Trabekulares Implantat mit Arzneistofffreisetzung zur Behandlung von Glaukoma
Implant trabeculaire a liberation de medicament pour le traitement du glaucome
PATENT ASSIGNEE:
Glaukos Corporation, (3911860), 26061 Merit Circle, 101, Laguna Hills, CA 92653, (US), (Applicant designated States: all)
INVENTOR:
Tu, Hosheng , 15 Riez, Newport Coast, California 92657, (US)
Niksch, Barbara, 28571 Jaeger Drive, Laguna Niguel, California 92677, (US)
Haffner, David, 24681 Via San Fernando, Mission Viejo, California 92692, (US)
Smedley, Gregory T., 81 Whitman Court, Irvine, California 92612, (US
LEGAL REPRESENTATIVE:
Hector, Annabel Mary et al (74722), D Young & Co., 21 New Fetter Lane, London EC4A 1DA, (GB)
PATENT (CC, No, Kind, Date): EP 1310222 A2 030514 (Basic)
EP 1310222 A3 040317
APPLICATION (CC, No, Date): EP 2002257644 021105;
PRIORITY (CC, No, Date): US 46137 011108
DESIGNATED STATES: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; SK; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS (V7): A61F-009/007; A61F-009/00
ABSTRACT EP 1310222 A2

A device and method are provided for improved treatment of elevated intraocular pressure due to glaucoma. A trabecular shunting device is adapted for implantation within the trabecular meshwork of an eye such that aqueous humor flows controllably from the anterior chamber of the eye to Schlemm's canal, bypassing the trabecular meshwork. The trabecular shunting device may utilize a quantity of pharmaceuticals effective in treating glaucoma, which are controllably released from the device into cells of the trabecular meshwork and/or Schlemm's canal. Depending upon

the specific treatment contemplated, pharmaceuticals may be utilized in conjunction with the trabecular shunting device such that aqueous flow either increases or decreases as desired. Placement of the trabecular shunting device within the eye, and release of a glaucoma medication therefrom, can arrest or slow the progression of glaucoma.

ABSTRACT WORD COUNT: 133
NOTE: Figure number on first page: 3
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200320	1100
SPEC A	(English)	200320	7742
Total word count - document A			8842
Total word count - document B			0
Total word count - documents A + B			8842

```
File 155:MEDLINE(R) 1950-2006/Jun 29
         (c) format only 2006 Dialog
File   5:Biosis Previews(R) 1969-2006/Jun W4
         (c) 2006 The Thomson Corporation
File  73:EMBASE 1974-2006/Jun 30
         (c) 2006 Elsevier Science B.V.
File  34:SciSearch(R) Cited Ref Sci 1990-2006/Jun W4
         (c) 2006 Inst for Sci Info
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
Set     Items   Description
S1        217   AU='TU H' OR AU='TU H.'
S2         84   AU='TU HOSHENG' OR AU='TU HR'
S3     197245   VASOMODULAT? OR VASOCONSTRICT? OR ALPHA(1W)AGONIST? OR TET-
              RACAINE OR BRIMONIDINE OR BETA()ADRENERGIC()ANTAGONIST?
S4          0   S1:S2 AND S3
S5     114343   GLAUCOMA
S6          3   S1:S2 AND S5
S7          3   RD  (unique items)
S8     255977   TOPICAL??
S9          0   S1:S2 AND S8

 7/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0015977989   BIOSIS NO.: 200600323384
Implant with pressure sensor for glaucoma treatment
AUTHOR: Gharib Morteza;  Tu Hosheng ; Bergheim Olav
AUTHOR ADDRESS: San Marino, CA USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office
Patents JAN 3 2006 2006
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: A trabecular shunt and methods for treating glaucoma are
  disclosed. One of the methods comprises transporting fluid from the
  anterior chamber of an eye to Schlemm's canal through an implant, the
  implant extending between the anterior chamber and Schlemm's canal;
  sensing an intraocular pressure using a sensor incorporated into the
  implant; and transmitting a signal indicative of the sensed pressure to
  an external receiver.


 7/7/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2006 The Thomson Corporation. All rts. reserv.
0014905990   BIOSIS NO.: 200400276747
 Glaucoma  treatment device
AUTHOR:  Tu Hosheng  (Reprint); Bergheim Olav G; Gharib Morteza
AUTHOR ADDRESS: Laguna Hills, CA, USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office
Patents  1282 (3): May 18, 2004 2004
MEDIUM: e-file
ISSN: 0098-1133 _(ISSN print)
DOCUMENT TYPE: Patent
```

RECORD TYPE: Abstract
LANGUAGE: English
ABSTRACT: A **glaucoma** treatment device for directing the flow of aqueous humor and bypassing trabecular meshwork is disclosed. The device comprises an inlet section, an outlet section, a middle section, and at least one lumen for transmitting aqueous humor within the **glaucoma** device. The lumen extends through at least one of the sections, and the outlet section is substantially perpendicular to the middle section, and fits within a conduit of aqueous humor outflow in the eye..

7/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014701215 BIOSIS NO.: 200400081972
Bifurcatable trabecular shunt for glaucoma **treatment**
AUTHOR: Gharib Morteza (Reprint); **Tu Hosheng** ; Bergheim Olav
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ABSTRACT: A trabecular shunt and methods for treating **glaucoma** are disclosed. The method comprises placing a trabecular shunt through diseased trabecular meshwork, between the anterior chamber and Schlemm's canal. The trabecular shunt includes a hollow, elongated tubular element having an inlet section and an outlet section. The outlet section includes two bifurcatable elements adapted to be positioned and stabilized inside Schlemm's canal.